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BUREAU OF COMMUNICABLE DISEASE CONTROL

M E M O R A N D U M

To: Obstetricians, gynecologists, nurse midwives, nurse practitioners, nurses

From: _____, Epidemiologist
Immunization Program (MIP)
Massachusetts Department of Public Health (MDPH)

Date: _____

Subj.: Diagnosis of rubella infection in pregnant women exposed to rubella and in their babies

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As you are probably aware, CRS occurs in up to 90% of infants born to women who are infected with rubella during the first trimester of pregnancy. When maternal infection occurs in the first half of pregnancy, 20%-25% of fetuses will be born with CRS. The most common congenital defects are cataracts, heart defects, sensorineural deafness, and developmental delay. Other problems include glaucoma, pigmentary retinopathy, microcephaly, meningoencephalitis, radiolucent bone defects, and liver or spleen involvement.

Although the risk of congenital defects decreases after the first trimester, CRS can occur with second trimester infection; sensorineural deafness has been noted even when infection occurs beyond 20 weeks gestation.

Although thought to be rare, instances of fetal infection and CRS caused by maternal reinfection during pregnancy have been documented, including one such occurrence in Massachusetts in 1994. Thus, preexisting evidence of rubella immunity, while reassuring, cannot be taken as a guarantee that an exposed pregnant woman and her fetus will be protected from infection.

Infected babies who appear normal at birth should be followed closely during the first few years of life, as congenital rubella-related defects such as deafness and cognitive/developmental problems may appear later. In addition, these normal-appearing infants may still be infectious.

The Massachusetts Department of Public Health (MDPH) provides the following recommendations regarding management of pregnant women exposed to rubella and their babies. These recommendations largely concern issues of **diagnosis**, which can be difficult given that rash is present in only about half of cases.

I. Diagnosis of rubella infection in pregnant women and those who have recently delivered

A. Pregnant woman exposed to rubella, regardless of symptoms

- Verify dates of rubella immunization and dates and results of serologic tests. Note that documentation of rubella immunization does **not** constitute proof of immunity for exposed pregnant women; immunity must be documented by a verified, dated record of a positive serology test. Nevertheless, it is important to collect documentation of prior rubella vaccination, because it serves to reduce the level of suspicion (and anxiety) that rubella infection occurred and it aids in the interpretation of the lab results.
- If a woman is susceptible (i.e., without pre-existing serologic evidence of immunity), draw blood specimens for rubella IgM and IgG serologic testing according to the following schedule:
  1st: as soon as possible after exposure; freeze an aliquot for possible repeat testing
  2nd: at 2-3 weeks after 1st, to be tested concurrently with 1st
  3rd: at 6 weeks after 1st, to be tested concurrently with 1st.
- If the outbreak (and potential for exposure) continues beyond this initial 6-week testing period, specimens should be collected from susceptible exposed pregnant women every 10-14 days if exposure continues, or every 3-4 weeks in situations of no known exposure, and tested together with the first specimen.
- If rash or rubella-like symptoms develop, even in a woman with pre-existing serologic evidence of immunity, collect a blood specimen at $\geq$ 3 days after rash onset.
- Send each specimen to the Massachusetts State Laboratory (MA SLI)—see attached protocol and requisition form.
- Interpret serologic results as follows:
  a) If either rubella IgM or a significant rise in rubella IgG is detected, the woman has been infected—no further serologic testing of her is necessary. Try to determine the timing of infection, if possible.
  b) If **all** the above serologic tests are **negative** for rubella IgM and there is no significant rise in rubella IgG, the woman may be assumed to have avoided infection. *However*, bear in mind that if the first blood was not collected until several weeks after exposure, it may not be possible to detect an infection resulting from it, as rubella IgM only stays elevated for about 6 weeks.
- If rubella infection in the mother was not reliably ruled out, follow and document the pregnancy outcome (e.g. termination, CRS, normal infant). The MIP will be contacting you to collect this information. Diagnostic testing of the baby will be necessary, as reflected below:

	Pregnant woman's lab results		
Possible conclusions	Rubella IgM-neg. and no rise in IgG	Rubella IgM-pos. or significant rise in IgG	Maternal infection neither confirmed nor ruled out prior to delivery
Woman infected?	No	Yes	Unknown
Need to follow baby?	No	Yes—see Section II	Yes—see Section II

Immune globulin (IG)
The use of IG for postexposure prophylaxis of rubella in early pregnancy does not guarantee prevention of fetal infection and is **not** routinely recommended.[1] Administration of IG should be considered only if termination of the pregnancy is not an option.

B. Woman possibly exposed to rubella during pregnancy but who was not tested before delivery

Regardless of whether symptoms were present, collect acute and convalescent sera for rubella IgM and IgG testing and send to MA SLI (see attached protocol and requisition form). If the acute specimen is positive for rubella IgM, this indicates that infection occurred and no further testing of the mother is necessary.

II. Diagnosis of rubella infection in infants born to women with confirmed or suspected rubella infection

- Regardless of the point in pregnancy at which infection is believed to have occurred, obtain laboratory confirmation (or rule-out) of fetal infection as follows:
    1. Collect specimens for virus isolation according to the attached protocol; 100% of congenitally infected newborns excrete rubella virus in nasopharyngeal secretions and urine at birth. Virus may be shed from the throat and urine for a year or longer. Specimens for virus isolation should be obtained at birth and every 1-2 months until two consecutive cultures are negative, at which point the baby can be assumed to be no longer infectious. This test is useful both for determining whether the infant is infectious as well as for diagnosing fetal infection—culture is the most sensitive diagnostic test in these infants.
    2. Collect serum specimen from infant (cord blood at birth is good) and send to SLI for rubella IgM testing—see attached protocol and requisition form. If positive for rubella IgM, fetal infection has occurred. 90-97% of CRS infants aged 2 weeks to 3 months have IgM, but only 80% of CRS babies are IgM positive by *some* laboratory tests, so a negative rubella IgM result by itself does not rule out the possibility of infection. Retesting is indicated if there is a high index of suspicion.

[1] Limited data indicate that IG in a dose of 0.55 ml/kg may prevent or modify infection in an exposed, susceptible person. In one study, the attack rate of clinically apparent infection was reduced from 87% in control subjects to 18% in recipients of IG. However, the absence of clinical signs in a woman who has received IG does not guarantee that fetal infection has been prevented. In this study, 44% of the IG recipients were infected. Infants with congenital rubella are known to have been born to mothers who were given IG shortly after exposure.

3. If infant is negative for rubella IgM at birth, collect another serum at age $\geq$ 3 months and another specimen 1 month later and send to SLI (with the specimen collected at birth, if available) for paired testing for rubella IgG. If only passive transfer of maternal IgG antibody has occurred, the baby's titer would be expected to drop at a rate of a 2-fold dilution per month. If fetal infection has occurred, the titer will persist and not drop as quickly.

- Pending laboratory confirmation (or rule-out), notify the pediatrician of the need for long term follow-up. As mentioned above, instances of deafness have been documented even when maternal infection occurs after 20 weeks gestation.

III. Rubella prevention and control

During outbreaks, advise susceptible pregnant women to avoid the affected setting(s) (e.g. schools, military settings, workplace, churches, athletic events, or other social gatherings).

Remember to evaluate all adults, especially women of childbearing age, for needed immunizations at every encounter with the health care system. Foreign-born adults without vaccination records should be vaccinated with MMR.

It is important to **vaccinate** all susceptible post-partum women **prior to discharge** from the hospital. (**Note:** Previous administration of human anti-Rho(D) immune globulin (RhoGam) does not generally interfere with an immune response to rubella vaccine. However, women who have received anti-Rho immune globulin should be serologically tested 6-8 weeks after vaccination to assure that seroconversion occurred. If other antibody-containing blood products are needed for other reasons, they should be administered at least 2 weeks before and deferred for up to 11 months after administration of MMR vaccine.)

State supplied MMR vaccine is available for use in the following groups and sites:

Availability of State-Supplied MMR Vaccine
• All children through 18 years of age in both public and private clinics • High-risk adults at over 450 public sites • Post-partum women at **all** maternity hospitals state-wide

The Massachusetts Immunization Program will provide detailed rubella infection control recommendations. Please call an Immunization Epidemiologist at 617-983-6800.

IV. REFERENCES

American Academy of Pediatrics. *Red Book*, 25th edition, 2000.

American College of Obstetricians and Gynecologists. Rubella and pregnancy. *Technical Bulletin*, no. 171, Aug. 1992.

Barfield, W, R Gardner, S Lett, C Johnsen. Congenital rubella reinfection in a mother with anti-cardiolipin and anti-platelet antibodies. *Pediatric Infectious Disease Journal* 16(2):249-251, 1997.

Best, JM, JE Banatvala, P Morgan-Capner, E Miller. Fetal infection after maternal reinfection with rubella: criteria for defining reinfection. *Brit. Med. J*. 299:773-775.

Centers for Disease Control and Prevention. Congenital rubella syndrome among the Amish—Pennsylvania, 1991-1992. *Morbidity and Mortality Weekly Report*, vol. 41, no. 26, July 3, 1992.

Centers for Disease Control and Prevention. *Manual for the Surveillance of Vaccine-Preventable Diseases*, Sept. 1997.

Cradock-Watson, JE, MKS Ridehalgh, MJ Anderson, and JR Pattison. Outcome of asymptomatic infection with rubella virus during pregnancy. *J. Hyg., Camb*. 87:174-154, 1981.

Miller, E. Rubella in the United Kingdom. *Epidemiol. Infect*. 107:31-42, 1991.

Miller, E., JE Cradock-Watson, TM Pollock. Consequences of confirmed maternal rubella at successive stages of pregnancy. *Lancet* 2(8302):781-784, 1982. Correction: *Lancet* (8305):998, 1982.

Morgan-Capner, P, E Miller, JE Vurdien, MEB Ramsay. Outcome of pregnancy after maternal reinfection with rubella. *Communicable Disease Report* (PHLS Communicable Disease Surveillance Centre, London) Review No. 6, 1991.

Robinson, J, M Lemay, WL Vaudry. Congenital rubella after anticipated maternal immunity: two cases and a review of the literature. *Pediatric Infectious Disease Journal* 13:812-815, 1994.

Zgorniak-Nowosielska, I., B. Zawilinska, & S. Szostek. Rubella infection during pregnancy in the 1985-86 epidemic: follow-up after seven years. *European Journal of Epidemiology* 12:303-308, 1996.

Attachments: Protocols and requisition form for serologic diagnostic testing and virus isolation